A novel application of cancer immunotherapy for autoimmune disease using engineered chimeric antigen receptor (CAR)-mesenchymal stem cells (MSCs).

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Multiple sclerosis (MS) is one of the most prevalent and debilitating neurological diseases affecting approximately 2.5 million people worldwide. MS is characterized by unpredictable immune-mediated attacks on the myelin sheath and nerve fibers affecting and inhibiting brain, spinal cord, and optic nerve functions of the central nervous system (CNS). Although there is currently no cure for this debilitating disease, there is a range of treatments including mesenchymal stem cell (MSC) therapy, which has been shown to inhibit immune pathways and support tissue repair. However, MSCs have complex and suboptimal biodistribution, limited specificity, and insufficient immunomodulatory effects. FDA-approved chimeric antigen receptor (CAR) T-cell therapy enabled previously non-functional T cells to become highly potent via CAR transgene transfer, causing unprecedented success in the treatment of hematological malignancies. By transducing MSCs to express a CAR, this study aims to increase the specificity and efficiency of MSC therapy, while broadening the application of CAR technology. This preliminary research 1) demonstrates a new lentiviral method to engineer and transduce MSCs, 2) identifies the optimal CD28 signaling pathway and Ad-MSC source to enhance the immunosuppressive properties of MSCs, and 3) applies preliminary findings as a cellular therapeutic strategy to autoimmune disorders including MS. The results presented in this study will guide future research in determining immunomodulatory mechanisms of CAR-MSCs, testing CAR constructs in vitro and in vivo, and engineering new ones relevant to other diseases. With the limited therapeutic options, this technology could be life-changing for patients with MS.

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